10/566,668

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=> d his

     (FILE 'HOME' ENTERED AT 12:51:16 ON 14 MAR 2007)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 12:51:48 ON 14 MAR 2007
L1        123475 S "BCL-2"
L2         32399 S ANTI(W)APOPTOTIC
L3          2888 S LIGAND AND L2
L4          1093 S L1 AND L3
L5       8223329 S CLON? OR EXPRESS? OR RECOMBINANT
L6           855 S L4 AND L5
L7        128710 S "BCL-X" OR "BCL-2" OR "BCL-W"
L8           855 S L6 AND L7
L9           557 S HUMAN AND L8
L10         4111 S HUMAN (2W)L1
L11           29 S L9 AND L10
L12           12 DUP REM L11 (17 DUPLICATES REMOVED)
                 E MALMAISON O G/AU
                 E HICKMAN J/AU
L13          256 S E3
                 E BENNET R/AU
L14          136 S E3
                 E RAIN J C/AU
L15           60 S E9
L16          452 S L13 OR L14 OR L15
L17            0 S L4 AND L16
L18            7 S L1 AND L16
L19            4 DUP REM L18 (3 DUPLICATES REMOVED)

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NEWS 3	OCT 23	The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
NEWS 4	OCT 30	CHEMLIST enhanced with new search and display field
NEWS 5	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS 6	NOV 10	CA/CAplus F-Term thesaurus enhanced
NEWS 7	NOV 10	STN Express with Discover! free maintenance release Version 8.01c now available
NEWS 8	NOV 20	CA/CAplus to MARPAT accession number crossover limit increased to 50,000
NEWS 9	DEC 01	CAS REGISTRY updated with new ambiguity codes
NEWS 10	DEC 11	CAS REGISTRY chemical nomenclature enhanced
NEWS 11	DEC 14	WPIDS/WPINDEX/WPIX manual codes updated
NEWS 12	DEC 14	GBFULL and FRFULL enhanced with IPC 8 features and functionality
NEWS 13	DEC 18	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS 14	DEC 18	CA/CAplus patent kind codes updated
NEWS 15	DEC 18	MARPAT to CA/CAplus accession number crossover limit increased to 50,000
NEWS 16	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS 17	DEC 27	CA/CAplus enhanced with more pre-1907 records
NEWS 18	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 19	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 20	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS 21	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 22	JAN 22	CA/CAplus updated with revised CAS roles
NEWS 23	JAN 22	CA/CAplus enhanced with patent applications from India
NEWS 24	JAN 29	PHAR reloaded with new search and display fields
NEWS 25	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 26	FEB 13	CASREACT coverage to be extended
NEWS 27	Feb 15	PATDPASPC enhanced with Drug Approval numbers
NEWS 28	Feb 15	RUSSIAPAT enhanced with pre-1994 records
NEWS 29	Feb 23	KOREAPAT enhanced with IPC 8 features and functionality
NEWS 30	Feb 26	MEDLINE reloaded with enhancements
NEWS 31	Feb 26	EMBASE enhanced with Clinical Trial Number field
NEWS 32	Feb 26	TOXCENTER enhanced with reloaded MEDLINE
NEWS 33	Feb 26	IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS 34	Feb 26	CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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 NEWS X25       X.25 communication option no longer available

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=> file medline embase biosis biotechds scisearch hcaplus ntis lifesci
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FILE 'LIFESCI' ENTERED AT 12:51:48 ON 14 MAR 2007
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=> s "bcl-2"
L1      123475 "BCL-2"

=> s anti(w)apoptotic
L2       32399 ANTI(W) APOPTOTIC

=> s ligand and l2
L3        2888 LIGAND AND L2

=> s l1 and l3
L4        1093 L1 AND L3

=> s clon? or express? or recombinant
L5     8223329 CLON? OR EXPRESS? OR RECOMBINANT
```

```
=> s l4 and l5
L6          855 L4 AND L5

=> s "BCL-X" or "bcl-2" or "bcl-W"
L7       128710 "BCL-X" OR "BCL-2" OR "BCL-W"

=> s l6 and l7
L8          855 L6 AND L7

=> s human and l8
L9          557 HUMAN AND L8

=> s human (2w)l1
L10        4111 HUMAN (2W) L1

=> s l9 and l10
L11          29 L9 AND L10

=> dup rem l11
PROCESSING COMPLETED FOR L11
L12          12 DUP REM L11 (17 DUPLICATES REMOVED)

=> d 1-12 ibib ab

L12  ANSWER 1 OF 12  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
ACCESSION NUMBER:    2007:25729  BIOSIS
DOCUMENT NUMBER:     PREV200700024836
TITLE:               M. leprae inhibits apoptosis in THP-I cells by
                     downregulation of Bad and Bak and upregulation of Mcl-I
                     gene expression.
AUTHOR(S):           Hasan, Zahra [Reprint Author]; Ashraf, Mussarat; Tayyebi,
                     Ali; Hussain, Rabia
CORPORATE SOURCE:    Aga Khan Univ, Dept Pathol and Microbiol, Karachi 74800,
                     Pakistan
                     zahra.hasan@aku.edu; mussaratashraf@yahoo.co.uk;
                     akhan52@hotmail.com; rabia.hussain@aku.edu
SOURCE:              BMC Microbiology, (SEP 18 2006) Vol. 6.
                     ISSN: 1471-2180.
DOCUMENT TYPE:       Article
LANGUAGE:            English
ENTRY DATE:          Entered STN: 27 Dec 2006
                     Last Updated on STN: 27 Dec 2006
AB   Background: Virulent Mycobacterium leprae interfere with host defense
     mechanisms such as cytokine activation and apoptosis.  The mitochondrial
     pathway of apoptosis is regulated by the Bcl-2 family
     of proteins.  Expression of Fas ligand and apoptotic
     proteins is found in leprosy lesions and M. leprae has been shown to
     activate pro-apoptotic Bcl-2 genes, Bak and Bax.
     However, the mechanism by which M. leprae modulates apoptosis is as yet
     unclear.  We investigated expression of apoptotic genes in THP-1
     monocytes in response to infection by M. leprae and non-pathogenic M.
     bovis BCG.Results: M. leprae did not induce apoptosis in THP-1 cells,
     while BCG induced a significant loss of cell viability by 18 h
     post-infection at both (multiplicity of infection) MOI-10 and 20, with an
     increase by 48 h.  BCG-induced cell death was accompanied by
     characteristic apoptotic DNA laddering in cells.  Non-viable BCG had a
     limited effect on host cell death suggesting that BCG-induced apoptosis
     was a function of mycobacterial viability.  M. leprae also activated lower
     levels of TNFalpha secretion and TNF-alpha mRNA expression than
     BCG.  Mycobacterium-induced activation of apoptotic gene
     expression was determined over a time course of infection.  M.
     leprae reduced Bad and Bak mRNA expression by 18 h
     post-stimulation, with a further decrease at 48 h.  Outcome of cell
```

viability is determined by the ratio between pro-and anti-apoptotic proteins present in the cell. M. leprae infection resulted in downregulation of gene expression ratios, Bad/Bcl-2 mRNA by 39% and Bak/Bcl-2 mRNA by 23%. In contrast, live BCG increased Bad/Bcl-2 mRNA (29%) but had a negligible effect on Bak/Bcl-2 mRNA. Heat killed BCG induced only a negligible (1-4%) change in mRNA expression of either Bak/Bcl-2 or Bad/Bcl-2. Additionally, M. leprae upregulated the expression of anti-apoptotic gene Mcl-1 while, BCG downregulated Mcl-1 mRNA.Conclusion: This study proposes an association between mycobacterium-induced apoptosis in THP-1 cells and the regulation of Bcl-2 family of proteins. M. leprae restricts apoptosis in THP-1 cells by downregulation of Bad and Bak and upregulation of Mcl-1 mRNA expression.

L12 ANSWER 2 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:74801 BIOSIS
DOCUMENT NUMBER: PREV200600073434
TITLE: Tissue microarray analysis of Fas and FasL expressions in human non-small cell lung carcinomas; with reference to the p53 and bcl-2 overexpressions.
AUTHOR(S): Myong, Na-Hye [Reprint Author]
CORPORATE SOURCE: Dankiik Univ, Coll Med, Dept Pathol, San 29 Anseo Dong, Cheonnan 330714, South Korea
myongnh@hanmail.net
SOURCE: Journal of Korean Medical Science, (OCT 2005) Vol. 20, No. 5, pp. 770-776.
CODEN: JKMSEH. ISSN: 1011-8934.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 19 Jan 2006
Last Updated on STN: 19 Jan 2006

AB Lack of surface Fas expression is a main route for apoptotic resistance which is considered an important mechanism of tumorigenesis and tumor progression. Fas and FasL expressions in 110 non-small cell lung carcinomas (NSCLCs) were investigated to evaluate their roles in pulmonary carcinogenesis and to examine the clink copathologic significance of Fas expression with its relationship with p53 and bcl-2 overexpressions. Immunohistochemical analysis using tissue microarray demonstrated that a large proportion of NSCLC patients (60%) showed lack of membranous Fas expression. The Fas-negative cases revealed the significantly lower survival rate than Fas-positive ones. Also, the loss of Fas receptor expression was found more frequently in advanced stage and higher nodal status. FasL protein was increased in most NSCLCs (89%) compared to normal lungs. p53 and bcl-2 overexpressions showed no association with Fas expression. Conclusively, reduced membranous Fas expression as a mechanism of apoptotic resistance is considered to play an important part of the pulmonary carcinogenesis, which may predict poor survival and have a bad prognostic influence. Increased FasL expression is thought to be a basis for the immune evasion in NSCLCs. The rare bcl-2 overexpression suggests that this anti-apoptotic protein is unlikely to play a role in the apoptotic resistance of NSCLCs.

L12 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:466192 HCAPLUS
DOCUMENT NUMBER: 137:42646
TITLE: A novel Bcl-2 homolog, Bcl-Rambo, involved in signal transduction in apoptosis induction and a cDNA encoding it
INVENTOR(S): Tschopp, Juerg; Hofmann, Kay

PATENT ASSIGNEE(S): Apotech Research & Development Ltd., Switz.
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002048353	A2	20020620	WO 2001-EP14597	20011212
WO 2002048353	A3	20021219		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10100280	A1	20020718	DE 2001-10100280	20010104
AU 2002029653	A5	20020624	AU 2002-29653	20011212
EP 1366071	A2	20031203	EP 2001-990551	20011212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004115667	A1	20040617	US 2003-450366	20031121
PRIORITY APPLN. INFO.:			DE 2000-10061766 A	20001212
			DE 2001-10100280 A	20010104
			WO 2001-EP14597 W	20011212

AB A cDNA for the apoptotic signal transduction protein (Bcl-Rambo) is cloned and characterized for use in manufacture of the protein and antibodies to the protein for use in the regulation of apoptosis. Related proteins carrying the BHNo domains of Bcl-Rambo are also covered by the invention. Expression systems for the gene may be used to screen for ligands of the protein that may be used to regulate apoptosis. Bcl-rambo is a structural homolog of the anti-apoptotic Bcl-2 protein family containing conserved Bcl-2 homol. (BH) motifs 1, 2, 3, and 4. In Bcl-rambo the C-terminal membrane anchor region is preceded by a unique 250 amino acid insertion containing two tandem repeats. No interaction of Bcl-rambo with either anti-apoptotic (Bcl-2, Bcl-xL, Bcl-2, A1, MCL-1, E1B-19K, and BHRF1) or pro-apoptotic (Bax, Bak, Bik, Bid, Bim, and Bad) members of the Bcl-2 family was observed In mammalian cells, Bcl-rambo was localized to mitochondria, and its overexpression induced apoptosis that is specifically blocked by the caspase inhibitors, IAPs. Inhibitors controlling upstream events of either the "death receptor" (FLIP, FADD-DN) or the "mitochondrial" pro-apoptotic pathway (Bcl-xL) had no effect. The Bcl-rambo cell death activity was induced by its membrane-anchored C-terminal domain and not by the Bcl-2 homol. region.

L12 ANSWER 4 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:368997 BIOSIS
DOCUMENT NUMBER: PREV200300368997
TITLE: Sensitization of Resistant Non Small Lung Tumors to Cancer Therapy.
AUTHOR(S): Okouoyo, Stella [Reprint Author]; Ucur, Esat [Reprint Author]; Mattern, Juergen [Reprint Author]; Debatin, Klaus-Michael [Reprint Author]; Herr, Ingrid [Reprint Author]
CORPORATE SOURCE: Division of Molecular Oncology/Pediatrics, German Cancer Research Center, Heidelberg, Germany
SOURCE: Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract

No. 5513. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.

DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 13 Aug 2003
Last Updated on STN: 13 Aug 2003

AB The development of resistance to chemotherapy is a major problem in the treatment of cancer. For many drugs, the mechanism of resistance is poorly understood. Several reports have suggested that apoptosis signaling by death receptors and mitochondria are the main effectors of drug induced cytotoxicity. Therefore, we examined in patient-derived non small lung tumors the functionality of the death receptor and mitochondrial death pathways. We detected in vivo and in vitro strongly impaired expression of CD95 and its ligand as well as diminished activity of caspase-8, -9 and -3. Concomitantly, the loss of the mitochondrial membrane potential following cancer therapy was impaired. Furthermore, anti-apoptotic genes such as Bcl-2, Bcl-xL and X-IAP were upregulated. Thus, multiple suicide molecules are affected simultaneously thereby mediating resistance. Our future studies focus on sensitization of resistand tumors by retrovirally mediated transfer of effector caspases in vivo using patient-derived lung tumor cells as xenograft tumor model.

L12 ANSWER 5 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:557407 BIOSIS

DOCUMENT NUMBER: PREV200100557407

TITLE: The differential sensitivity of Bcl-2-overexpressing human breast tumor cells to TRAIL or doxorubicin-induced apoptosis is dependent on Bcl-2 protein levels.

AUTHOR(S): Ruiz de Almodovar, Carmen; Ruiz-Ruiz, Carmen; Munoz-Pinedo, Cristina; Robledo, Gema; Lopez-Rivas, Abelardo [Reprint author]

CORPORATE SOURCE: Instituto de Parasitologia y Biomedicina CSIC, calle Ventanilla 11, 18001, Granada, Spain
alrivas@ipb.csic.es

SOURCE: Oncogene, (25 October, 2001) Vol. 20, No. 48, pp. 7128-7133. print.
CODEN: ONCNES. ISSN: 0950-9232.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 5 Dec 2001
Last Updated on STN: 25 Feb 2002

AB Bcl-2 protein is a potent anti-apoptotic protein that inhibits a mitochondria-operated pathway of apoptosis in many cells. DNA damaging agents and death receptor ligands can activate this mitochondrial apoptotic mechanism. Tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) has been suggested to escape from the inhibitory action of Bcl-2 protein. We show that in human breast tumor MCF-7 cells, TRAIL induced a mitochondrial pathway of apoptosis that involved cytochrome c release from mitochondria and activation of caspase 9. The DNA damaging drug doxorubicin also activated this mitochondria-regulated mechanism of apoptosis, which was inhibited in Bcl-2-overexpressing cells. We also demonstrate that in MCF-7 cells Bcl-2 might confer resistance to TRAIL-induced apoptosis, depending on the expression levels of the anti-apoptotic protein. These results indicate that enhanced expression of Bcl-2 in tumor cells can render these cells less sensitive not only to chemotherapeutic drugs but also to TRAIL.

L12 ANSWER 6 OF 12 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2001514930 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11562676
TITLE: Adenovirus-mediated Bcl-2 gene transfer inhibits apoptosis and promotes survival of allogeneic transplanted hepatocytes.
AUTHOR: Song E; Chen J; Antus B; Su F; Wang M; Exton M S
CORPORATE SOURCE: Department of Hepatobiliary Surgery, Sun-Yat-Sen Memorial Hospital, Sun-Yat-Sen University of Medical Science, Guangzhou, People's Republic of China.
SOURCE: Surgery, (2001 Sep) Vol. 130, No. 3, pp. 502-11.
Journal code: 0417347. ISSN: 0039-6060.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20 Sep 2001
Last Updated on STN: 15 Oct 2001
Entered Medline: 11 Oct 2001

AB BACKGROUND: Donor hepatocyte apoptosis that is induced by host cytotoxic T lymphocytes (CTLs) limits the application of hepatocyte transplantation. Hepatocytes from Bcl-2 transgenic mice can resist the lethal effect of anti-Fas antibody. However, the anti-apoptotic effect of Bcl-2 expression on allogeneic transplanted hepatocytes remains elusive. This study tested the feasibility of Bcl-2 gene transfer as an approach to inhibit CTL-mediated apoptosis in allogeneic transplanted hepatocytes. METHODS: An adenovirus vector that encoded human Bcl-2 gene (AdCMVhBcl-2) was used to transfect cultured rat hepatocytes, which were then transplanted into allogeneic spleens. DNA fragmentation and caspase-3 activation were examined by terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate nick end-labeling assay and immunohistochemistry for active caspase-3, respectively. Cocultivation of hepatocytes and allogeneic CD8(+) T lymphocytes was performed, and cytotoxicity on hepatocytes was examined by alanine transaminase release. RESULTS: Bcl-2 gene transfer inhibited apoptosis and increased liver-associated enzyme activities in allogeneic transplanted hepatocytes, which were associated with inhibition of caspase-3 activation. Alanine transaminase release in hBcl-2 modified hepatocytes was lower compared with controls, which could not be further decreased by inhibition of Fas ligand and granzyme B. CONCLUSIONS: Adenovirus-mediated Bcl-2 gene transfer blocks CTL-mediated apoptosis in allogeneic hepatocytes by inhibition of caspase-3 activation. Bcl-2 gene transfer could be used to promote survival of transplanted hepatocytes.

L12 ANSWER 7 OF 12 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2000076282 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10607745
TITLE: Transgenic overexpression of human Bcl-2 in islet beta cells inhibits apoptosis but does not prevent autoimmune destruction.
AUTHOR: Allison J; Thomas H; Beck D; Brady J L; Lew A M; Elefanty A; Kosaka H; Kay T W; Huang D C; Strasser A
CORPORATE SOURCE: The Walter and Eliza Hall Institute for Medical Research, Post Office, Royal Melbourne Hospital, Victoria 3050, Australia.
SOURCE: International immunology, (2000 Jan) Vol. 12, No. 1, pp. 9-17.
Journal code: 8916182. ISSN: 0953-8178.
PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 9 Mar 2000
Last Updated on STN: 9 Mar 2000
Entered Medline: 24 Feb 2000

AB Insulin-dependent diabetes mellitus results when > 90% of the insulin-producing beta cells in the pancreatic islets are killed as a result of autoimmune attack by T cells. During the progression to diabetes, islet beta cells die as a result of different insults from the immune system. Agents such as perforin and granzymes, CD95 ligand and tumor necrosis factor-alpha, or cytokines and free-radicals have all been shown to cause beta cell apoptosis. The anti-apoptotic protein, Bcl-2, might protect against some of these stimuli. We have therefore generated transgenic mice expressing human Bcl-2 in their islet beta cells. Although Bcl-2 was able to prevent apoptosis induced by cytotoxic agents against beta cells in vitro, Bcl-2 alone could not prevent or ameliorate cytotoxic or autoimmune beta cell damage in vivo.

L12 ANSWER 8 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:168915 BIOSIS
DOCUMENT NUMBER: PREV199900168915
TITLE: The implications of proliferation and apoptosis for lung cancer metastasis.
AUTHOR(S): Volm, Manfred [Reprint author]; Koomaegi, Reet
CORPORATE SOURCE: Dep. 0511, German Cancer Res. Cent., Im Neuenheimer Feld 280, D-69120 Heidelberg, Germany
SOURCE: Oncology Reports, (March-April, 1999) Vol. 6, No. 2, pp. 373-376. print.
ISSN: 1021-335X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 19 Apr 1999
Last Updated on STN: 19 Apr 1999

AB The occurrence of metastatic spread depends on many factors both the condition of the patient and the properties of the tumor. In this investigation the association between proliferation and apoptosis and the incidence of lymph node involvement of patients with non-small cell lung carcinomas was analysed (n=215 patients). In order to analyse the relationship between lymph node metastasis and proliferative activity of the carcinomas, the distribution of cell cycle phases (flow cytometry), the expression of PCNA and cyclin A (immunohistochemistry) was determined. Fas, Fas-ligand, caspase-3 and Bcl-2 were determined by immunohistochemistry. In this retrospective analysis no association between proliferative activity of the tumors and lymph node status was found. In contrast, there existed a correlation between the apoptotic factors and lymph node metastasis. Higher expression of the pro-apoptic factors Fas, Fas-ligand and caspase-3 correlated with a lower incidence of lymph node involvement (Fas-ligand, p=0.004; caspase-3, p=0.007). The trend of an inverse correlation between the anti-apoptotic factor Bcl-2 and metastasis fits well into the present knowledge about the function of the bcl-2 gene. The results obtained from all the patients could be confirmed in patients with squamous cell lung carcinomas.

L12 ANSWER 9 OF 12 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 1998400472 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9731746
TITLE: Withdrawal of 2-mercaptoethanol induces apoptosis in a

B-cell line via Fas upregulation.
AUTHOR: Neumann D; Zierke M; Martin M U
CORPORATE SOURCE: Institute for Clinical Molecular Pharmacology, Medical School, Hannover, Germany.. biology@dompe.it
SOURCE: Journal of cellular physiology, (1998 Oct) Vol. 177, No. 1, pp. 68-75.
Journal code: 0050222. ISSN: 0021-9541.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 6 Oct 1998
Last Updated on STN: 6 Oct 1998
Entered Medline: 21 Sep 1998

AB Mouse lymphoid cell cultures are dependent on reducing agents in their culture medium to allow proliferation and survival of the cells. In the case of the mouse CD5+-pre-B cell line SPGM-1, withdrawal of 2-mercaptoethanol (2-ME) resulted in rapid inhibition of proliferation and subsequent cell death by apoptosis. The pathways leading to cell death by withdrawal of 2-ME or by incubation with ionomycin, a known inducer of apoptosis, were compared. Both kinds of stimulation resulted in apoptosis of the whole population, but cell death occurred with different kinetics. Only apoptosis induced by ionomycin was inhibited by coincubation with the phorbol ester PMA, while apoptosis induced by withdrawal of 2-ME was not. Overexpression of the human bcl-2 proto-oncogene in these cells delayed the death process induced by either method. SPGM-1xbcl-2 cells accumulated in the G0/G1 and G2/M cell cycle phases after removal of 2-ME from the medium, whereas treatment with ionomycin resulted in an arrest only in the G0/G1 transition. Interestingly, both stimuli induced the expression of the Fas receptor, but with different kinetics, while the Fas ligand (FasL) was expressed constitutively in SPGM-1 cells. These data demonstrate that withdrawal of 2-ME and incubation with ionomycin both induce rapid cell death by apoptosis, possibly mediated by an autocrine Fas/FasL loop. Although the initial pathways activated by the two forms of treatment must be different, they converge on a common level controlled by the anti-apoptotic gene product Bcl-2.

L12 ANSWER 10 OF 12 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 96135169 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8564847
TITLE: Bcl-2 protects from lethal hepatic apoptosis induced by an anti-Fas antibody in mice.
AUTHOR: Lacronique V; Mignon A; Fabre M; Viollet B; Rouquet N; Molina T; Porteu A; Henrion A; Bouscary D; Varlet P; Joulin V; Kahn A
CORPORATE SOURCE: Institut Cochin de Genetique Moleculaire, U 129 INSERM, Universite Rene Descartes, Paris, France.
SOURCE: Nature medicine, (1996 Jan) Vol. 2, No. 1, pp. 80-6.
Journal code: 9502015. ISSN: 1078-8956.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199603
ENTRY DATE: Entered STN: 15 Mar 1996
Last Updated on STN: 3 Mar 2000
Entered Medline: 5 Mar 1996

AB Fas is an apoptosis-signalling cell surface antigen that has been shown to trigger cell death upon specific ligand or antibody binding.

Treatment of mice with an anti-Fas antibody causes fulminant hepatic failure due to massive apoptosis. To test a putative protective effect of the anti-apoptotic Bcl-2 protein, transgenic mice were generated to express the human bcl-2 gene product in hepatocytes. Early onset of massive hepatic apoptosis leading to death was observed in all nontransgenic mice treated with an anti-Fas antibody. By contrast, hepatic apoptosis was delayed and dramatically reduced in transgenic animals, yielding a 93% survival rate. These results demonstrate that Bcl-2 is able to protect from in vivo Fas-mediated cytotoxicity, and could be of significance for preventing fulminant hepatic failure due to viral hepatitis in humans.

L12 ANSWER 11 OF 12 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
ACCESSION NUMBER: 1996-02155 BIOTECHDS
TITLE: Transfection of eukaryotic cells;
with an adeno virus vector and polycation conjugate;
long-lasting expression in gene therapy by
apoptosis-inhibitor and antiinflammatory gene transfer
AUTHOR: Cotten M; Baker A; Chiocca S
PATENT ASSIGNEE: Boehr.Ingelheim
LOCATION: Ingelheim am Rhein, Germany.
PATENT INFO: WO 9533062 7 Dec 1995
APPLICATION INFO: WO 1995-EP1989 26 May 1995
PRIORITY INFO: DE 1994-4442587 30 Nov 1994; DE 1994-444258P 30 Nov 1994
DOCUMENT TYPE: Patent
LANGUAGE: German
OTHER SOURCE: WPI: 1996-030572 [03]
AB A new process for introducing foreign material, e.g. nucleic acid, into higher eukaryote cells, involves introduction of the material and transfection components, introducing 1 or more DNA fragments whose expression products at least partially block apoptosis induced by introduction of foreign material (e.g. human Bcl-2, adeno virus E1B 19K or a p53-inactivator), and/or at least partially inhibiting the inflammatory response by external treatment with an antiinflammatory or introducing an antiinflammatory gene into cells (e.g. an adeno virus VA1 protein, a phospholipase-A2-inhibitor, glucocorticoid, dexamethasone, or a prostaglandin-antagonist). A DNA fragment of 1929 bp and a protein of 283 amino acids are specified. A new transfection complex contains target nucleic acid, complexed with a polycation optionally conjugated with a target cell ligand, an adeno virus or adeno virus-polycation conjugate, and anti-apoptotic DNA and/or antiinflammatory DNA. Suppression of apoptosis and/or inflammation allows longer-lasting expression of foreign nucleic acids in human cells, e.g. in the context of gene therapy. (100pp)

L12 ANSWER 12 OF 12 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
ACCESSION NUMBER: 1996-02136 BIOTECHDS
TITLE: Transfection of eukaryotic cells;
in the presence of anti-apoptotic
and/or antiinflammatory
AUTHOR: Cotten M; Baker A
PATENT ASSIGNEE: Boehr.Ingelheim
LOCATION: Ingelheim, Germany.
PATENT INFO: DE 4418825 7 Dec 1995
APPLICATION INFO: DE 1994-4418825 30 May 1994
PRIORITY INFO: DE 1994-4418825 30 May 1994
DOCUMENT TYPE: Patent
LANGUAGE: German
OTHER SOURCE: WPI: 1996-021085 [03]
AB A process is claimed for introducing foreign material, e.g. nucleic acid, into higher eukaryotic cells, by introducing the foreign material and transfection components into the cells and (a) introducing 1 or more

nucleic acid (especially DNA) molecules whose expression products at least partially block apoptosis induced by introduction of the foreign material, and/or (b) at least partially inhibiting the inflammatory response of the cells by (i) treating the cells externally with 1 or more antiinflammatory (AI) substances and/or (ii) introducing 1 or more AI substances, or nucleic acid (especially DNA) molecules coding for such substances into the cells. Also claimed is a transfection complex comprising (1) a nucleic acid molecule to be expressed in a target cell, where the nucleic acid is complexed with a polycation and the polycation is optionally conjugated with a ligand for the target cells, (2) an adeno virus or an adeno virus-polycation conjugate, and (3) a DNA molecule with anti-apoptotic activity and/or a DNA molecule coding for a substance with AI activity. The nucleic acid codes for human Bcl-2, adeno viral E1B 19K or a gene product that inactivates p53. (23pp)

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E7            1      MALMAKOV N/AU
E8            2      MALMAKOV N I/AU
E9            1      MALMAKOV NURLAN/AU
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E12           1      MALMAN JOHAN/AU

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=> e bennet r/au
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E12           1      BENNET R J L/AU

=> s e3
L14         136 "BENNET R"/AU
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E7            2     RAIN J S/AU
E8            1     RAIN JC/AU
E9           60     RAIN JEAN CHRISTOPHE/AU
E10           3     RAIN JEAN D/AU
E11           1     RAIN JEAN DIDER/AU
E12          58     RAIN JEAN DIDIER/AU

=> s e9
L15          60 "RAIN JEAN CHRISTOPHE"/AU

=> d his

     (FILE 'HOME' ENTERED AT 12:51:16 ON 14 MAR 2007)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 12:51:48 ON 14 MAR 2007
L1        123475 S "BCL-2"
L2         32399 S ANTI(W)APOPTOTIC
L3          2888 S LIGAND AND L2
L4          1093 S L1 AND L3
L5       8223329 S CLON? OR EXPRESS? OR RECOMBINANT
L6           855 S L4 AND L5
L7        128710 S "BCL-X" OR "BCL-2" OR "BCL-W"
L8           855 S L6 AND L7
L9           557 S HUMAN AND L8
L10         4111 S HUMAN (2W)L1
L11           29 S L9 AND L10
L12           12 DUP REM L11 (17 DUPLICATES REMOVED)
                 E MALMAISON O G/AU
                 E HICKMAN J/AU
L13          256 S E3
                 E BENNET R/AU
L14          136 S E3
                 E RAIN J C/AU
L15           60 S E9

=> s l13 or l14 or l15
L16          452 L13 OR L14 OR L15

=> s l4 and l16
L17            0 L4 AND L16

=> s l1 and l16
L18            7 L1 AND L16

=> dup rem l18
PROCESSING COMPLETED FOR L18
L19            4 DUP REM L18 (3 DUPLICATES REMOVED)

=> d 1-4 ibib ab

L19   ANSWER 1 OF 4  BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
      DUPLICATE 1
ACCESSION NUMBER: 2006-21503  BIOTECHDS
TITLE:            Peptide interacting with anti-apoptotic members of
                  Bcl-2 protein family useful for the
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treatment of cancers,;
protein interaction and recombinant vector expression in host cell for disease therapy
AUTHOR: GENESTE O; HICKMAN J; RAIN J C
PATENT ASSIGNEE: LES LAB SERVIER SA; HYBRIGENICS
PATENT INFO: FR 2881430 4 Aug 2006
APPLICATION INFO: FR 2005-978 1 Feb 2005
PRIORITY INFO: FR 2005-978 1 Feb 2005; FR 2005-978 1 Feb 2005
DOCUMENT TYPE: Patent
LANGUAGE: French
OTHER SOURCE: WPI: 2006-571572 [59]
AB DERWENT ABSTRACT:
NOVELTY - A peptide interacting with members of the anti-apoptotic Bcl-2 protein family comprising a fully defined 24 amino acid sequence (SEQ ID NO. 1-6) given in the specification, or their functional variants, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for: (1) nucleic acid sequences encoding the peptide; (2) a recombinant vector comprising the nucleic acid sequence; (3) a host cell comprising the vector; (4) a pharmaceutical composition comprising the peptide; and (5) identifying (M1) modulators of the interaction of the peptide and an anti-apoptotic Bcl-2 family member comprising: (a) contacting the peptide with an anti-apoptotic Bcl-2 family member; (b) adding the test compound; and (c) measuring the activity of the test compound which modulates interaction between the peptide and anti-apoptotic Bcl-2 family member and comparing it to a measurment taken in the absence of the test compound.
BIOTECHNOLOGY - Preferred Nucleic Acid Sequence: The nucleic acids comprise (SEQ ID NO. 7-11) fully defined in the specification. Preferred Vector: The vector is a plasmid, cosmid, artificial bacterial chromosome or a bacteriophage comprising the sequences necessary for the expression of the peptide, under the control of a promoter of transcription and/or transduction. Preferred Host Cell: The host cell is a bacteria or a eukaryotic cell. Preferred Method: (M1) also comprises: (a) marking the peptide with a fluorescent marker; (b) incubating the peptide in the presence of the test compound; (c) adding the anti-apoptotic Bcl -2 family member; (d) measuring the polarisation of fluorescence; and (e) comparing the measurement with and without the test compound. The modulator increases or diminishes the amount of polarization of fluorescence. The fluorescent probe is fluorescein. The anti-apoptotic Bcl-2 family member is particularly Bcl-2, Bcl-XL or Bcl-W.
ACTIVITY - Cytostatic; Apoptotic. No biological data given.
MECHANISM OF ACTION - None given.
USE - The peptide is useful in a pharmaceutical composition used for treating cancer by inducing programmed cell death (claimed). (41 pages)

L19 ANSWER 2 OF 4 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
DUPLICATE 2
ACCESSION NUMBER: 2006-21502 BIOTECHDS
TITLE: Identifying modulators of programmed cell death, useful for treating cancer, comprising interacting the motif of beclin protein and anti-apoptotic member of the Bcl-2, Bcl-XL/Bcl-W protein family;
programmed cell death modulator identification and vector expression host cell for use in disease therapy
AUTHOR: GENESTE O; HICKMAN J; RAIN J C
PATENT ASSIGNEE: LES LAB SERVIER SA; HYBRIGENICS
PATENT INFO: FR 2881429 4 Aug 2006
APPLICATION INFO: FR 2005-977 1 Feb 2005
PRIORITY INFO: FR 2005-977 1 Feb 2005; FR 2005-977 1 Feb 2005
DOCUMENT TYPE: Patent
LANGUAGE: French
OTHER SOURCE: WPI: 2006-571571 [59]

AB DERWENT ABSTRACT:
NOVELTY - Identifying modulators of programmed cell death, comprising interacting the motif of beclin protein and anti-apoptotic member of Bcl-2, Bcl-XL/Bcl-W protein family and detecting the interaction optionally in presence of a compound to be tested, is new.

DETAILED DESCRIPTION - Identifying modulators of programmed dead cells, comprising interacting the motif of beclin protein and anti-apoptotic member of Bcl-2, Bcl-XL/Bcl-W protein family and detecting the interaction optionally in presence of a compound, is new. The motif comprises Gly-Thr-Met-Glu-Asn-Leu-Ser-Arg-Arg-Leu-Lys-Val-Thr-Gly-Asp-Leu-Phe-Asp-Ile-Met-Ser-Gly-Gln-Thr-Asp-Val (SEQ ID NO. 1). INDEPENDENT CLAIMS are included for: (1) a sequence of amino acids comprising (SEQ ID NO. 1); (2) a nucleic acid sequence (SEQ ID NO. 2) encoding the amino acid sequence of (1); (3) a nucleic acid sequence deduced from the genetic code of (SEQ ID NO. 1); (4) a recombinant vector comprising the nucleic acid sequence of (2);(5) a host cell transformed by the vector of (5); (6) a peptide comprising (SEQ ID NO. 1); (7) a peptide encoded by (SEQ ID NO. 2) or the nucleic acid sequence of (3); (5) a pharmaceutical composition comprising the peptide of (6) or (7).

BIOTECHNOLOGY - Preferred Method: The method further comprises marking the motif by fluorescein; adding an anti-apoptotic member to the motif; incubating the system; measuring of the fluorescence polarization; and comparing the measurement with or without the compound to be tested. The interaction is an inhibitor decreasing or an activator increasing the fluorescence polarizations. The anti-apoptotic member is a member of the Bcl-2 family of proteins, particularly Bcl-2, Bcl-XL or Bcl-W. Preferred Vector: The vector is a plasmid, a cosmid, an artificial bacterial chomosome or a bacteriophage comprising the sequences necessary for the expression of the Beclin protein motif, including a promoter sequence of transcription and transduction.

ACTIVITY - Cytostatic; Apoptotic. No biological data given.

MECHANISM OF ACTION - None given.

USE - The pharmaceutical composition is useful as an inductor of apoptotic and/or autophagic cell death for treating cancer (claimed).(35 pages)

L19 ANSWER 3 OF 4 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
DUPLICATE 3
ACCESSION NUMBER: 2005-09128 BIOTECHDS
TITLE: New peptide that binds Bcl-2 and Bcl-XL, useful in screening for modulators of apoptosis, potentially useful for treating e.g., autoimmune diseases and cancer; recombinant protein production via plasmid expression in host cell for use in disease therapy
AUTHOR: GENESTE O; HICKMAN J; BENNETT R; RAIN J C
PATENT ASSIGNEE: LES LAB SERVIER SA; HYBRIGENICS
PATENT INFO: FR 2858621 11 Feb 2005
APPLICATION INFO: FR 2003-9697 6 Aug 2003
PRIORITY INFO: FR 2003-9697 6 Aug 2003; FR 2003-9697 6 Aug 2003
DOCUMENT TYPE: Patent
LANGUAGE: French
OTHER SOURCE: WPI: 2005-155005 [17]
AB DERWENT ABSTRACT:
NOVELTY - A peptide (I) that interacts with the antiapoptotic proteins Bcl-2 and/or Bcl-XL, is new.

DETAILED DESCRIPTION - A peptide (I) that interacts with the antiapoptotic proteins Bcl-2 and/or Bcl-XL, is new. INDEPENDENT CLAIMS are also included for: (1) a peptide (Ia) that is a fragment or point mutant of (I); (2) a nucleic acid sequence (II) encoding (I); 5'-GATACCCGTCGCAGCATGGTGTTTGCCAGGCACCTGCGGGAGGTGGGAGACGAGTTCAGGAGCAGA-3' (2); (3) a deduced nucleic acid sequence (IIa) for (I) and (Ia); (4) a recombinant (expression) vector that contains (II) or (IIa); (5) a host cell transformed by the vector of (4); and (6) identifying molecules (III) that modulate the interaction between (I) or (Ia) and an

antiapoptotic protein. Asp-Thr-Arg-Arg-Ser-Met-Val-Phe-Ala-Arg-His-Leu-Arg-Glu-Val-Gly-Asp-Glu-Phe-Arg-Ser-Arg (I); 5'-GATACCCGTCGCAGCATGGTGTTTGCCAGGCACCTGCGGGAGGTGGGAGACGAGTTCAGGAGCAGA-3' (II);

BIOTECHNOLOGY - Preferred Process: In identifying molecules that modulate the interaction between (I) or (Ia) and an antiapoptotic protein a fluorescently labeled (I) or (Ia) is incubated with a test compound, a fusion protein containing the antiapoptotic protein is added and fluorescence polarization is measured. Compounds that reduce the fluorescence polarization are inhibitors of the interaction and compounds which increase fluorescence polarization are promoters of the interaction. Preferred labels are Oregon Green, bodipy and fluorescein (most preferred). Isolation: (I) was identified in a two hybrid assay, using Bcl-2/-XL as the bait and human cDNA banks as prey. Its ability to induce apoptosis was confirmed by transformation/microinjection of cells.

ACTIVITY - Cytostatic; Immunosuppressive; Neuroprotective; Apoptotic; Antiapoptotic.

MECHANISM OF ACTION - Bcl-2 modulator; Bcl-XL modulator; Apoptosis modulator.

USE - (I), and its fragments and point mutants, are used to identify molecules that modulate apoptosis and/or are useful in treating diseases that involve deregulation of apoptosis, particularly autoimmune diseases, some (degenerative) neurological diseases and cancer (claimed).

ADVANTAGE - Since (I) is a small peptide, it is ideally suited for high efficiency screening for modulators of protein interactions. (23 pages)

L19 ANSWER 4 OF 4 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1994:220230 SCISEARCH
THE GENUINE ARTICLE: NE758
TITLE: CHARACTERIZATION OF RADIATION-INDUCED APOPTOSIS IN THE SMALL-INTESTINE AND ITS BIOLOGICAL IMPLICATIONS
AUTHOR: POTTEN C S (Reprint); MERRITT A; HICKMAN J; HALL P; FARANDA A
CORPORATE SOURCE: CHRISTIE HOSP & HOLT RADIUM INST, PATERSON INST CANC RES, CRC, DEPT EPITHELIAL BIOL, WILMSLOW RD, MANCHESTER M20 9BX, LANCS, ENGLAND (Reprint); UNIV MANCHESTER, SCH BIOL SCI, CRC, MOLEC & CELLULAR PHARMACOL GRP, MANCHESTER M13 9PT, LANCS, ENGLAND; ST THOMAS HOSP, DEPT HISTOPATHOL, LONDON SE1 7EH, ENGLAND
COUNTRY OF AUTHOR: ENGLAND
SOURCE: INTERNATIONAL JOURNAL OF RADIATION BIOLOGY, (JAN 1994) Vol. 65, No. 1, pp. 71-78.
ISSN: 0955-3002.
PUBLISHER: TAYLOR & FRANCIS LTD, ONE GUNDPOWDER SQUARE, LONDON, ENGLAND EC4A 3DE.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 34
ENTRY DATE: Entered STN: 1994
Last Updated on STN: 1994

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The small intestine with its high cell proliferation, well-accepted hierarchy, high radiation susceptibility and low cancer incidence is a useful model for studying the controls of cell replacement. Apoptosis, which represents part of the overall homeostatic process, occurs spontaneously at the stem cell position in the crypts, and very small doses of radiation elevate the levels of apoptosis rapidly in this region. Other cytotoxic agents also target cells in this region including several mutagenic chemicals. Yet other drugs target cells at higher positions in the crypt indicating that all crypt cells possess the programme for

apoptosis, but this is normally suppressed in many of the cells. In contrast, high doses of radiation are required to reproductively sterilize the crypts and, using clonal regeneration techniques, the number of clonogenic cells is dependent on the levels of damage induced (dose), i.e. the more injury that is induced the greater number of cells that are recruited into the clonogenic compartment. All doses of radiation trigger rapid changes in proliferation in the stem cell region which suggests that the detection of the induced cell death (even small levels, such as one apoptotic cell per crypt) is efficient and has rapid consequences, p53 may be involved in this damage recognition and apoptosis initiation. The studies to date suggest that apoptosis plays an important role in this tissue in terms of its homeostasis and its protection against carcinogenesis by removal of potentially carcinogenic damaged cells.

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(FILE 'HOME' ENTERED AT 12:51:16 ON 14 MAR 2007)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 12:51:48 ON 14 MAR 2007

L1	123475	S	"BCL-2"
L2	32399	S	ANTI(W)APOPTOTIC
L3	2888	S	LIGAND AND L2
L4	1093	S	L1 AND L3
L5	8223329	S	CLON? OR EXPRESS? OR RECOMBINANT
L6	855	S	L4 AND L5
L7	128710	S	"BCL-X" OR "BCL-2" OR "BCL-W"
L8	855	S	L6 AND L7
L9	557	S	HUMAN AND L8
L10	4111	S	HUMAN (2W)L1
L11	29	S	L9 AND L10
L12	12	DUP REM	L11 (17 DUPLICATES REMOVED)
		E	MALMAISON O G/AU
		E	HICKMAN J/AU
L13	256	S	E3
		E	BENNET R/AU
L14	136	S	E3
		E	RAIN J C/AU
L15	60	S	E9
L16	452	S	L13 OR L14 OR L15
L17	0	S	L4 AND L16
L18	7	S	L1 AND L16
L19	4	DUP REM	L18 (3 DUPLICATES REMOVED)

	Issue Date	Pages	Document ID	Title
1	20070215	31	US 20070036775 A1	Method of modulating or examining Ku70 levels in cells
2	20070201	16	US 20070027169 A1	XIAP-Targeted Prostate Cancer Therapy
3	20070201	125	US 20070026076 A1	Molecular vaccines employing nucleic acid encoding anti-apoptotic proteins
4	20061228	48	US 20060292178 A1	Proteins encoded by the severe acute respiratory syndrome (SARS) coronavirus and a role in apoptosis
5	20061214	111	US 20060280749 A1	Therapeutic agents comprising pro-apoptotic proteins
6	20061207	60	US 20060275294 A1	METHOD OF PREVENTION AND TREATMENT OF AGING, AGE-RELATED DISORDERS AND/OR AGE-RELATED MANIFESTATIONS INCLUDING ATHEROSCLEROSIS, PERIPHERAL VASCULAR DISEASE, CORONARY ARTERY DISEASE, OSTEOPOROSIS, ARTHRITIS, TYPE 2 DIABETES, DEMENTIA, ALZHEIMERS DISEASE AND CANCER
7	20061123	25	US 20060263809 A1	Method for sensitive measure of low level apoptosis in cells
8	20061123	123	US 20060263368 A1	Targeted chimeric molecules for cancer therapy
9	20061116	35	US 20060257401 A1	Sensitizing cells for apoptosis by selectively blocking cytokines

	Issue Date	Pages	Document ID	Title
10	20061109	44	US 20060252801 A1	Small molecule Bcl-xL/Bcl-2 binding inhibitors
11	20061102	44	US 20060247305 A1	Chromen-4-one inhibitors of anti-apoptotic Bcl-2 family members and the uses thereof
12	20061026	71	US 20060241290 A1	Sequences characteristic of hypoxia-regulated gene transcription
13	20061026	71	US 20060241033 A1	Markers for pre-cancer and cancer calls and the method to interfere with cell proliferation therein
14	20061012	45	US 20060228799 A1	Use of consensus sequences for targeted homologous gene isolation and recombination in gene families
15	20060824	47	US 20060188948 A1	Methods for identifying agents that modulate apoptosis in cells that over-express a Bcl-2 family member protein
16	20060817	10	US 20060183688 A1	Peptide interacting with anti-apoptotic proteins of the bcl-2 family
17	20060817	64	US 20060183687 A1	Novel therapeutic molecules
18	20060810	30	US 20060178435 A1	Apogossypolone and the uses thereof
19	20060803	19	US 20060172414 A1	Feeder layer and serum independent embryonic stem cells

	Issue Date	Pages	Document ID	Title
20	20060720	78	US 20060159654 A1	Protein belonging to the TNF superfamily involved in signal transduction, nucleic acids encoding same, and methods of use thereof
21	20060706	40	US 20060148700 A1	Methods and compositions for reducing injury to a transplanted organ
22	20060615	46	US 20060127928 A1	Targeted therapy marker panels
23	20060525	13	US 20060111288 A1	Peripheral benzodiazepine receptor independent superoxide generation
24	20060525	34	US 20060110735 A1	Use of molecular markers for the preclinical and clinical profiling of inhibitors of enzymes having histone deacetylase activity
25	20060511	22	US 20060099194 A1	Composition and method for clusterin-mediated stem cell therapy for treatment of atherosclerosis and heart failure
26	20060420	27	US 20060084697 A1	Pi3k antagonists as radiosensitizers
27	20060420	131	US 20060084647 A1	Small molecule inhibitors of anti-apoptotic BCL-2 family members and the uses thereof

28	20060420	134	US 20060084621 A1	Compositions and methods for inhibiting expression of anti-apoptotic genes

	Issue Date	Pages	Document ID	Title
29	20060413	59	US 20060078533 A1	Method of prevention and treatment of aging and age-related disorders including atherosclerosis, peripheral vascular disease, coronary artery disease, osteoporosis, arthritis, type 2 diabetes, dementia, alzheimer's disease and cancer
30	20060406	187	US 20060073474 A1	Methods and compositions for detecting the activation state of multiple proteins in single cells
31	20060323	66	US 20060062074 A1	Method for intracellular modifications within living cells using pulsed electric fields
32	20060316	49	US 20060058253 A1	Methods to reprogram splice site selection in pre-messenger rnas
33	20060316	25	US 20060057721 A1	Method of screening cell death modulators
34	20060316	41	US 20060057109 A1	Method of using anti-apoptotic factors in gene expression
35	20060223	23	US 20060040331 A1	Methods of screening apoptosis modulating compounds, compounds identified by said methods and use of said compounds as therapeutic agents

	Issue Date	Pages	Document ID	Title
36	20060105	59	US 20060002895 A1	Induction of apoptic or cytotoxic gene expression by adenoviral mediated gene codelivery
37	20051229	77	US 20050287545 A1	Protein belonging to the TNF superfamily involved in signal transduction, nucleic acids encoding same, and methods of use thereof
38	20051208	55	US 20050272682 A1	SiRNA targeting PI3K signal transduction pathway and siRNA-based therapy
39	20051208	31	US 20050272129 A1	Transgenic fungi expressing Bcl-2 and methods of using Bcl-2 or portions thereof for improving biomass production, survival, longevity and stress resistance of fungi
40	20051201	28	US 20050267128 A1	Compounds, compositions and methods of modulating the mitochondrial apoptosis-induced channel (MAC)
41	20051103	48	US 20050244844 A1	Methods of screening of PP1-interacting polypeptides or proteins, peptides inhibiting PP1c binding to Bcl-2 proteins, Bcl-xL and Bcl-w, and uses thereof
42	20051027	37	US 20050239873 A1	2 Methoxy antimycin a derivatives and methods of use

	Issue Date	Pages	Document ID	Title
43	20051020	21	US 20050234135 A1	Gossypol co-crystals and the use thereof
44	20051013	407	US 20050227917 A1	Gene products differentially expressed in cancerous cells and their methods of use II
45	20051006	198	US 20050222029 A1	Compositions and methods for treating diseases
46	20050922	53	US 20050208033 A1	Lactic acid bacteria and their use for treating and preventing cancer
47	20050811	114	US 20050176667 A1	Compositions and methods for inhibiting expression of anti-apoptotic genes
48	20050728	50	US 20050164970 A1	Method for treating prostate cancer using siRNA duplex for androgen receptor
49	20050728	55	US 20050164284 A1	Methods and compositions for detecting CDN apoptosis-modulating proteins
50	20050630	23	US 20050142621 A1	Methods of identifying anti-cancer agents and uses thereof
51	20050623	29	US 20050136492 A1	Affinity labeling of enzymes for detection of enzyme activity level in living cells

52	20050609	331	US 20050124010 A1	Whole cell engineering by mutagenizing a substantial portion of a starting genome combining mutations and optionally repeating

	Issue Date	Pages	Document ID	Title
53	20050602	54	US 20050119456 A1	PROTEIN THAT MODULATES THE STABILITY OF TRANSCRIPTIONAL REGULATORY COMPLEXES REGULATING NUCLEAR HORMONE RECEPTOR ACTIVITY, DNA ENCODING SAME, AND ANTIBODIES THERETO
54	20050602	85	US 20050118154 A1	Antitumor effect of mutant Bik
55	20050526	42	US 20050113351 A1	Prevention of ovarian cancer by administration of products that induce biologic effects in the ovarian epithelium
56	20050526	48	US 20050113305 A1	Compounds and methods for modulating cell-adhesion mediated drug resistance
57	20050324	45	US 20050064593 A1	Bcl-2-modifying factor (bmf) sequences and their use in modulating apoptosis
58	20050303	181	US 20050049399 A1	Novel molecules of the card-related protein family and uses thereof
59	20050224	22	US 20050043215 A1	Complex drug delivery composition and method for treating cancer
60	20050203	28	US 20050027000 A1	Methods and compounds useful to induce apoptosis in cancer cells
61	20050203	31	US 20050026201 A1	Method of modulating or examining Ku70 levels in cells

	Issue Date	Pages	Document ID	Title
62	20041230	156	US 20040265300 A1	Chimeric molecules containing a module able to target specific cells and a module regulating the apoptogenic function of the permeability transition pore complex (PTPC)
63	20041216	26	US 20040253629 A1	Mammalian pro-apoptotic bok genes and their uses
64	20041216	57	US 20040253245 A1	Modulators
65	20041202	21	US 20040242526 A1	Disruption of the REG pathway
66	20041202	37	US 20040241657 A1	Liver related disease compositions and methods
67	20041111	19	US 20040223971 A1	Composition and uses of galectin antagonists
68	20041028	143	US 20040214902 A1	Small molecule antagonists of BCL-2 family proteins
69	20040923	34	US 20040185043 A1	Hematopoietic stem cell chimerism to treat autoimmune disease
70	20040916	36	US 20040180846 A1	Connexin enhances chemotherapy-induced apoptiosis in human cancer cells inhibiting tumor cell proliferation
71	20040909	43	US 20040176336 A1	Prevention of ovarian cancer by administration of products that induce biologic effects in the ovarian epithelium

72	20040902	44	US 2004017180 9 A1	BH3 peptides and method of use thereof

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73	20040812	64	US 20040157327 A1	Pablo, a polypeptide that interacts with BCL-XL, and uses related thereto
74	20040701	51	US 20040127685 A1	Novel molecules of the card-related protein family and uses thereof
75	20040701	45	US 20040126879 A1	Heart derived cells for cardiac repair
76	20040603	41	US 20040106587 A1	Prevention of ovarian cancer by administration of products that induce biologic effects in the ovarian epithelium
77	20040513	46	US 20040091885 A1	Use of consensus sequences for targeted homologous gene isolation and recombination in gene families
78	20040506	13	US 20040086495 A1	Method for the treatment of arteriosclerosis
79	20040422	379	US 20040077090 A1	Whole cell engineering by mutagenizing a substantial portion of a starting genome, combining mutations, and optionally repeating
80	20040415	51	US 20040072342 A1	Production and use of microvessels in fibronectin-containing gel

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81	20040415	34	US 20040072146 A1	Mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of screening active molecules having the ability to alter and/or prevent and/or mimic the interaction of Vpr with ANT
82	20040318	38	US 20040054129 A1	Novel peptides and compositions which modulate apoptosis
83	20040311	24	US 20040048823 A1	Anticancer agent comprising mycolactone
84	20040226	57	US 20040039212 A1	Sphingolipid derivatives and their methods of use
85	20040205	41	US 20040023866 A1	Bacterial BCL-2 domain-containing polypeptides, encoding nucleic acid molecules, and related methods
86	20031106	39	US 20030207933 A1	Compositions and methods for increasing the sensitivity of apoptosis-resistant tumor cells to inducers of apoptosis
87	20031023	43	US 20030199489 A1	Small molecule inhibitors targeted at BCL-2
88	20031009	58	US 20030190709 A1	Pablo, a polypeptide that interacts with Bcl-xL, and uses related thereto

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89	20031002	69	US 20030185820 A1	Protein belonging to the TNF superfamily involved in signal transduction, nucleic acids encoding same, and methods of use thereof
90	20030925	59	US 20030180740 A1	Differential expression screening method
91	20030918	71	US 20030176506 A1	Induction of apoptosis in cancer cells
92	20030911	77	US 20030171279 A1	Methods and composition concerning herpesvirus Us3 and BAD-involved apoptosis
93	20030911	69	US 20030170898 A1	Method for intracellular modifications within living cells using pulsed electric fields
94	20030724	78	US 20030139344 A1	Antitumor activity of Bok
95	20030724	47	US 20030139331 A1	Treatment of cancer by reduction of intracellular energy and pyrimidines
96	20030710	85	US 20030130222 A1	Antisense modulation of BH3 interacting domain death agonist expression
97	20030703	33	US 20030124505 A1	High-throughput gene cloning and phenotypic screening
98	20030626	179	US 20030120055 A1	Novel molecules of the card-related protein family and uses thereof

99	20030508	111	US 2003008691 9 A1	Therapeutic agents comprising pro-apoptotic proteins

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100	20030501	34	US 20030083301 A1	Therapeutic treatments for spinal cord injury via blockade of interleukin-1 receptor
101	20030501	52	US 20030082551 A1	High-throughput gene cloning and phenotypic screening
102	20030424	47	US 20030078210 A1	Compounds and methods for modulating cell-adhesion mediated drug resistance
103	20030424	51	US 20030077826 A1	Chimeric molecules containing a module able to target specific cells and a module regulating the apoptogenic function of the permeability transition pore complex (PTPC)
104	20030417	31	US 20030073661 A1	Method of modulating or examining Ku70 levels in cells
105	20030123	34	US 20030017196 A1	Oligonucleotide inhibitors of bcl-xL
106	20030109	49	US 20030008924 A1	Small molecule antagonists of Bcl-2 family proteins
107	20030109	39	US 20030008837 A1	Novel apoptosis-modulating proteins, DNA encoding the proteins and methods of use thereof
108	20030102	47	US 20030004140 A1	Methods for modulating cell-adhesion mediated drug resistance

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111	20020926	51	US 20020137049 A1	Pablo, a polypeptide that interacts with Bcl-xL, and uses related thereto
112	20020912	49	US 20020128219 A1	Novel molecules of the card related protein family and uses thereof
113	20020912	43	US 20020128198 A1	Novel molecules of the card-related protein family and uses thereof
114	20020815	10	US 20020110869 A1	Polynucleotide encoding chimeric protein and related vector, cell and method of expression thereof
115	20020808	40	US 20020106735 A1	Novel Bcl-2 related proline rich protein (BPR)
116	20020801	72	US 20020103353 A1	Sequences characteristic of hypoxia-regulated gene transcription
117	20020711	22	US 20020090374 A1	CHIMERIC PROTEINS WITH CELL-TARGETING SPECIFICITY AND APOPTOSIS-INDUCING ACTIVITIES
118	20020627	85	US 20020082228 A1	Antisense modulation of BH3 interacting domain death agonist expression

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119	20020620	20	US 20020076794 A1	Mammalian pro-apoptotic Bok genes and their uses
120	20020523	108	US 20020061845 A1	Novel molecules of the card-related protein family and uses thereof
121	20020523	35	US 20020061530 A1	Enhanced targeting of DNA sequences by recombinase protein and single-stranded homologous DNA probes using DNA analog activation
122	20020425	50	US 20020049173 A1	Alteration of cellular behavior by antisense modulation of mRNA processing
123	20011122	41	US 20010044431 A1	Prevention of ovarian cancer by administration of products that induce biologic effects in the ovarian epithelium
124	20011011	34	US 20010029013 A1	Bcl-G polypeptides, encoding nucleic acids and methods of use
125	20060919	55	US 7108989 B2	Apoptosis-modulating proteins, DNA encoding the proteins and methods of use thereof
126	20060905	110	US 7101977 B2	Therapeutic agents comprising pro-apoptotic proteins
127	20060829	37	US 7097982 B2	Peptides and compositions which modulate apoptosis
128	20060711	68	US 7074895 B2	Sequences characteristic of hypoxia-regulated gene transcription
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130	20060620	63	US 7064193 B1	Therapeutic molecules
131	20060620	74	US 7063960 B2	Protein belonging to the TNF superfamily involved in signal transduction, nucleic acids encoding same, and methods of use thereof
132	20060530	69	US 7053071 B2	Induction of apoptosis in cancer cells
133	20060425	345	US 7033781 B1	Whole cell engineering by mutagenizing a substantial portion of a starting genome, combining mutations, and optionally repeating
134	20060328	55	US 7019119 B2	Protein belonging to the TNF superfamily involved in signal transduction, nucleic acids encoding same, and methods of use thereof
135	20060103	52	US 6982317 B2	C21 polypeptide that modulates the stability of transcriptional regulatory complexes regulating nuclear hormone receptor activity
136	20051115	375	US 6964868 B1	Human genes and gene expression products II
137	20051011	58	US 6953657 B2	Molecules of the CARD-related protein family and uses thereof

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139	20050531	54	US 6900015 B2	Measurement of protective genes in allograft rejection
140	20050531	53	US 6899870 B1	Induction of apoptic or cytotoxic gene expression by adenoviral mediated gene codelivery
141	20050322	175	US 6869775 B2	Card related protein and uses thereof
142	20050208	59	US 6852691 B1	Anti-angiogenic peptides and methods of use thereof
143	20041102	51	US 6812003 B2	Compounds and methods for modulating cell-adhesion mediated drug resistance
144	20041005	50	US 6800750 B1	Mc1-1 gene regulatory elements and a pro-apoptotic mc1-1 variant
145	20040824	25	US 6780604 B2	Mammalian pro-apoptotic Bok genes and their uses
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147	20040330	31	US 6713280 B1	Enhancement of peptide cellular uptake
148	20031216	54	US 6664068 B2	Pablo, a polypeptide that interacts with Bcl-xL, and uses related thereto
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153	20030527	50	US 6570002 B1	Inhibitor of programmed cell death
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155	20030408	35	US 6544972 B1	Methods of limiting apoptosis of cells
156	20030225	44	US 6524856 B1	Use of consensus sequences for targeted homologous gene isolation and recombination in gene families
157	20021210	38	US 6492389 B1	Small molecule inhibitors of BCL-2 proteins
158	20021119	174	US 6482933 B1	Molecules of the card-related protein family and uses thereof
159	20021029	10	US 6472176 B2	Polynucleotide encoding chimeric protein and related vector, cell, and method of expression thereof
160	20021022	75	US 6468547 B1	Enhancement of tumor cell chemosensitivity and radiosensitivity using single chain secretory antibodies
161	20020820	26	US 6437097 B1	Mammalian pro-apoptotic Bok genes and their uses

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164	20020423	25	US 6376247 B1	Mammalian pro-apoptotic Bok genes and their uses
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168	20010424	25	US 6222017 B1	Mammalian pro-apoptotic Bok genes and their uses
169	20010424	37	US 6221615 B1	Peptides and compositions which modulate apoptosis
170	20010403	39	US 6210892 B1	Alteration of cellular behavior by antisense modulation of mRNA processing
171	20010123	24	US 6177259 B1	Assays and kits for inhibition of polyglutamine-induced cell death
172	20001010	27	US 6130317 A	Bax inhibitor proteins
173	20000613	62	US 6074640 A	Enhancement of tumor cell radiosensitivity using single chain intracellular antibodies
174	20000502	47	US 6057132 A	Nucleotide sequences encoding apoptosis associated Bbk protein

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175	20000328	25	US 6043055 A	Mammalian pro-apoptotic Bok genes and their uses
176	20000118	50	US 6015687 A	Apoptosis-modulating proteins, DNA encoding the proteins and methods of use thereof
177	19991207	68	US 5998583 A	BH3 interacting domain death agonist
178	19990921	68	US 5955593 A	BH3 interacting domain death agonist
179	19990629	15	US 5917124 A	Transgenic mouse model of prostate cancer
180	19990126	29	US 5863795 A	Nucleic acids that encode peptides which modulate apoptosis
181	19981117	28	US 5837838 A	Bax inhibitor proteins
182	19981110	51	US 5834234 A	Apoptosis associated protein Bbk
183	19980623	43	US 5770443 A	Apoptosis-modulating proteins, DNA encoding the proteins and methods of use thereof
184	19970930	48	US 5672686 A	Bcl-Y - specific antibodies
185	19970812	30	US 5656725 A	Peptides and compositions which modulate apoptosis

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1	20061207	60	US 20060275294 A1	METHOD OF PREVENTION AND TREATMENT OF AGING, AGE-RELATED DISORDERS AND/OR AGE-RELATED MANIFESTATIONS INCLUDING ATHEROSCLEROSIS, PERIPHERAL VASCULAR DISEASE, CORONARY ARTERY DISEASE, OSTEOPOROSIS, ARTHRITIS, TYPE 2 DIABETES, DEMENTIA, ALZHEIMERS DISEASE AND CANCER
2	20061123	123	US 20060263368 A1	Targeted chimeric molecules for cancer therapy
3	20060817	10	US 20060183688 A1	Peptide interacting with anti-apoptotic proteins of the bcl-2 family
4	20060413	59	US 20060078533 A1	Method of prevention and treatment of aging and age-related disorders including atherosclerosis, peripheral vascular disease, coronary artery disease, osteoporosis, arthritis, type 2 diabetes, dementia, alzheimer's disease and cancer
5	20060406	187	US 20060073474 A1	Methods and compositions for detecting the activation state of multiple proteins in single cells
6	20060316	41	US 20060057109 A1	Method of using anti-apoptotic factors in gene expression

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7	20051208	31	US 20050272129 A1	Transgenic fungi expressing Bcl-2 and methods of using Bcl-2 or portions thereof for improving biomass production, survival, longevity and stress resistance of fungi
8	20051013	407	US 20050227917 A1	Gene products differentially expressed in cancerous cells and their methods of use II
9	20050609	331	US 20050124010 A1	Whole cell engineering by mutagenizing a substantial portion of a starting genome combining mutations and optionally repeating
10	20050602	54	US 20050119456 A1	PROTEIN THAT MODULATES THE STABILITY OF TRANSCRIPTIONAL REGULATORY COMPLEXES REGULATING NUCLEAR HORMONE RECEPTOR ACTIVITY, DNA ENCODING SAME, AND ANTIBODIES THERETO
11	20041202	37	US 20040241657 A1	Liver related disease compositions and methods
12	20040902	44	US 20040171809 A1	BH3 peptides and method of use thereof

13	20040422	379	US 20040077090 A1	Whole cell engineering by mutagenizing a substantial portion of a starting genome, combining mutations, and optionally repeating

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14	20030918	71	US 20030176506 A1	Induction of apoptosis in cancer cells
15	20030724	47	US 20030139331 A1	Treatment of cancer by reduction of intracellular energy and pyrimidines
16	20020808	40	US 20020106735 A1	Novel Bcl-2 related proline rich protein (BPR)
17	20020425	50	US 20020049173 A1	Alteration of cellular behavior by antisense modulation of mRNA processing
18	20060530	69	US 7053071 B2	Induction of apoptosis in cancer cells
19	20060425	345	US 7033781 B1	Whole cell engineering by mutagenizing a substantial portion of a starting genome, combining mutations, and optionally repeating
20	20060103	52	US 6982317 B2	C21 polypeptide that modulates the stability of transcriptional regulatory complexes regulating nuclear hormone receptor activity
21	20051115	375	US 6964868 B1	Human genes and gene expression products II
22	20010403	39	US 6210892 B1	Alteration of cellular behavior by antisense modulation of mRNA processing
23	20010123	24	US 6177259 B1	Assays and kits for inhibition of polyglutamine-induced cell death

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1	L1	1	"20030032157".pn.
2	L2	5424	"Bcl-2"
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